ABCL–475

Five-year analysis of the POLARIX study: Prolonged follow-up confirms positive impact of polatuzumab vedotin plus rituximab, cyclophosphamide, doxorubicin, and prednisone (Pola-R-CHP) on outcomes

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Summary

In the **POLARIX study**, **Pola-R-CHP** showed a significant **PFS benefit** versus R-CHOP in patients with intermediate- or high-risk DLBCL.

At the 5-year follow-up, **consistently sustained and significant PFS and DFS benefits** were observed for patients receiving Pola-R-CHP versus R-CHOP, with **no new safety signals.**

Five-year data confirm **Pola-R-CHP as a standard of care** for patients with previously untreated intermediate- or high-risk DLBCL; **prolonged follow-up of POLARIX is planned.**

Fewer subsequent anti-lymphoma treatments were needed, and **numerically fewer deaths**, in particular lymphoma-related deaths, were observed in patients receiving **Pola-R-CHP** versus R-CHOP.

Data previously presented at the 66th American Society of Hematology (ASH) Annual Meeting, December 7–10, 2024

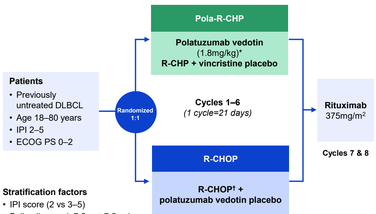
Background

- In the POLARIX study (NCT03274492; median follow-up 28 months), Pola-R-CHP showed a significant progression-free survival (PFS) benefit versus R-CHOP in patients with intermediate- or high-risk diffuse large B-cell lymphoma (DLBCL).[1]
- Here, we report outcomes after 5 years of follow-up (cut-off: July 5, 2024).

Methods

- POLARIX methods were published previously;[1] briefly, patients (18–80 years) were randomized 1:1 to receive 6 cycles of Pola-R-CHP or R-CHOP, plus 2 cycles of rituximab (**Figure 1**).
- In this analysis, 1000 patients (expanded population) were evaluated; 879 patients (global intention-to-treat [ITT] population) from the main study and 121 patients from a Chinese extension cohort.[2]

Figure 1. POLARIX study design.



*IV on D1; †R-CHOP: IV rituximab 375mg/m², cyclophosphamide 750mg/m², doxorubicin 50mg/m², and vincristine 1.4mg/m² (max. 2mg) on D1, plus oral prednisone 100mg once daily on D1–5. BICR, blinded independent central review; CR, complete response; D, Day; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS$_{ext}$, event-free survival (efficacy); EOT, end of treatment; INV, investigator; IPI, International Prognostic Index; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

Patient baseline characteristics in the global population

- Baseline characteristics are shown in **Table 1**.
- In the global ITT population, 879 (Pola-R-CHP, n=440; R-CHOP, n=439) and 873 patients (Pola-R-CHP, n=435; R-CHOP, n=438) were evaluable for efficacy and safety, respectively.
- In the expanded population, 1000 (Pola-R-CHP, n=500; R-CHOP, n=500) and 993 patients (Pola-R-CHP, n=495; R-CHOP, n=498) were evaluable for efficacy and safety, respectively.

Table 1. Patient baseline characteristics in the global ITT population.

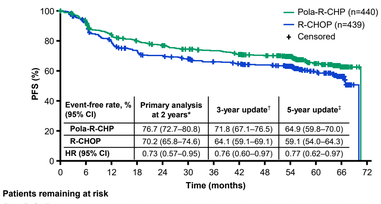
n (%), unless otherwise stated		Pola-R-CHP (n=440)	R-CHOP (n=439)
Age	Median, years (min–max) ≥65 years	65.0 (19–80) 231 (52.5)	66.0 (19–80) 236 (53.8)
Sex	Male	239 (54.3)	234 (53.3)
ECOG PS	0–1 2	374 (85.0) 66 (15.0)	363 (82.7)* 75 (17.1)
IPI at screening	2 3–5	167 (38.0) 273 (62.0)	167 (38.0) 272 (62.0)
Bulky disease	≥7.5cm	193 (43.9)	192 (43.7)
Baseline LDH	>1x upper limit of normal	291 (66.1)	284 (64.7)
Ann Arbor stage	III or IV	393 (89.3)	387 (88.2)
Number of extranodal sites	≥2	213 (48.4)	213 (48.5)
NHL histologic diagnosis reported by investigators	DLBCL, ABC, GCB HGBCL, DHL/THL Other large B-cell lymphoma	373 (84.8)† 43 (9.8) 24 (5.5)	367 (83.6) 50 (11.4) 22 (5.0)
COO centrally reported by NanoString‡	n ABC by NanoString GCB by NanoString Unclassified by NanoString Unknown	330 102 (30.9) 184 (55.8) 44 (13.3) 110	338 119 (35.2) 168 (49.7) 51 (15.1) 101

*ECOG PS was not reported for one patient in the R-CHOP arm; †The total percentage for NHL histologic diagnosis in the Pola-R-CHP arm may exceed 100% due to rounding; ‡Based on central review, and percentages are based on biomarker evaluable population (i.e., by excluding patients with unknown status). ABC, activated B cell; COO, cell-of-origin; DHL, double-hit lymphoma; GCB, germinal center B cell; HGBL, high-grade B-cell lymphoma; NHL, non-Hodgkin lymphoma; n, number; THL, triple-hit lymphoma.

Efficacy outcomes in the global ITT population at 5-year follow-up

- Pola-R-CHP had a sustained and significant PFS benefit (**Figure 2**), confirming results from the primary analysis of PFS at 2 years of follow-up.[1]

Figure 2. PFS in the global ITT population.



Event-free rate, % (95% CI)	Primary analysis at 2 years*	3-year update†	5-year update‡
Pola-R-CHP	76.7 (72.7–80.8)	71.8 (67.1–76.5)	64.9 (59.8–70.0)
R-CHOP	70.2 (65.8–74.6)	64.1 (59.1–69.1)	59.1 (54.0–64.3)
HR (95% CI)	0.73 (0.57–0.95)	0.76 (0.60–0.97)	0.77 (0.62–0.97)

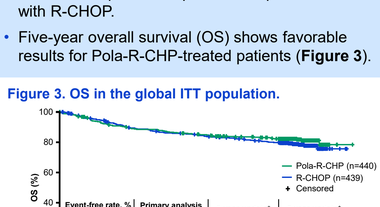
Patients remaining at risk

Pola-R-CHP	440	407	357	335	318	303	292	280	258	213	100	56	NE
R-CHOP	439	391	332	302	287	274	258	251	240	192	95	54	NE

*Data cut-off: June 28, 2021; †Data cut-off: June 15, 2022; ‡Data cut-off: July 5, 2024.
CI, confidence interval; HR, hazard ratio; NE, not evaluable.

- Complete remission obtained after Pola-R-CHP treatment is maintained at 5-year follow-up
  - The 5-year disease-free survival (DFS) estimates were 71.8% (95% confidence interval [CI]: 66.4–77.3) versus 66.5% (95% CI: 60.8–72.1) with Pola-R-CHP versus R-CHOP (HR 0.75; 95% CI: 0.57–1.00).
- Patients treated with Pola-R-CHP required 23% fewer subsequent therapies versus patients treated with R-CHOP.
- Five-year overall survival (OS) shows favorable results for Pola-R-CHP-treated patients (**Figure 3**).

Figure 3. OS in the global ITT population.



Event-free rate, % (95% CI)	Primary analysis at 2 years*	3-year update†	5-year update‡
Pola-R-CHP	88.7 (85.7–91.7)	85.6 (82.3–88.9)	82.3 (78.7–85.9)
R-CHOP	88.6 (85.6–91.6)	85.6 (82.2–88.9)	79.5 (75.7–83.4)
HR (95% CI)	0.94 (0.65–1.37)	0.94 (0.67–1.33)	0.85 (0.63–1.15)

Patients remaining at risk

Pola-R-CHP	440	424	399	389	381	373	366	355	343	338	319	124	12	1	NE
R-CHOP	439	415	403	382	372	361	357	347	338	329	311	128	13	1	NE

Data cut-off: June 28, 2021; *Data cut-off: June 15, 2022; †Data cut-off: July 5, 2024.

- In the global population, deaths associated with lymphoma progression are numerically fewer with Pola-R-CHP versus R-CHOP.
- Five-year PFS and OS outcomes show consistent treatment effect of Pola-R-CHP across subgroups in the global population
  - However, subgroup analyses are exploratory and generally underpowered, and should be interpreted with caution.

Efficacy outcomes in the expanded population at 5-year follow up

- Efficacy outcomes in the expanded population were similar to the global population (**Table 2**).

Table 2. Efficacy outcomes in the expanded population.

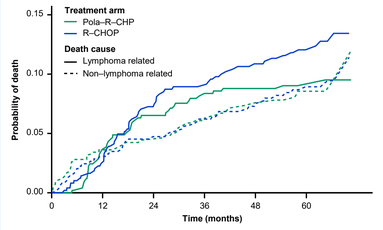
Efficacy analyses	Pola-R-CHP	R-CHOP
PFS analysis, n	500	500
Patients with PFS event, n (%)	163 (32.6)	189 (37.8)
Stratified HR (95% CI)	0.80 (0.65–0.98)	
DFS analysis, n	439	419
Patients remaining in CR, n (%)	327 (74.5)	292 (69.7)
Unstratified HR (95% CI)	0.81 (0.63–1.05)	
OS analysis, n	500	500
Patients with OS event, n (%)	88 (17.6)	104 (20.8)
Stratified HR (95% CI)	0.83 (0.62–1.10)	

Data cut off: July 5, 2024. DFS, disease-free survival.

Competing risk analysis for deaths in the expanded population

- In a competing risk analysis, the cumulative incidence of lymphoma-related deaths at 5 years was lower in patients treated with Pola-R-CHP versus R-CHOP (9.02% vs 12.05%; **Figure 4**).

Figure 4. Cumulative incidence of deaths due to lymphoma and other causes.

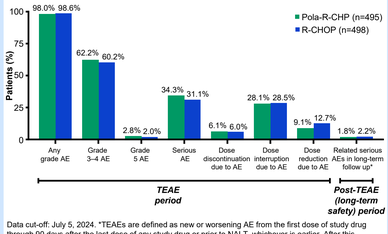


Competing risks for deaths were defined as deaths due to non-lymphoma related causes that prevent lymphoma-related deaths from occurring.

Safety summary in the expanded population

- Safety data were largely unchanged since prior analyses.[1,2]
- Safety profiles were comparable between treatment arms, with no increased risks with long term follow-up (**Figure 5**).

Figure 5. Safety summary in the expanded population.



Data cut-off: July 5, 2024. *TEAEs are any worsening AE from the first dose of study drug through 90 days after the last dose of any study drug or prior to NALT, whichever is earlier. After this TEAE period, the post-TEAE period (i.e. long-term safety follow up) reporting requirement is only for serious AEs that the investigator believes to be related to prior study drug treatment.
TEAE, treatment-emergent adverse event; NALT, new anti-lymphoma treatment.

- There was a <5% difference in hematological toxicities and infections in the Pola-R-CHP versus R-CHOP arm
  - For Pola-R-CHP versus R-CHOP, infections occurred in 47.9% versus 44.0% of patients; neutropenia in 48.5% versus 45.8%; anemia in 33.3% versus 30.1%; and thrombocytopenia in 18.0% versus 17.3%.
- Fewer secondary malignancies were observed with Pola-R-CHP versus R-CHOP.
- Rates of peripheral neuropathy were similar between treatment arms.

Conclusions

- The 5-year extended follow-up of POLARIX showed sustained and significant PFS and DFS benefits for patients receiving Pola-R-CHP versus R-CHOP, with no new safety signals were identified.
- Fewer subsequent anti-lymphoma treatments were needed with Pola-R-CHP versus R-CHOP.
- Numerically fewer deaths, in particular lymphoma-related deaths, were observed in patients receiving Pola-R-CHP compared with R-CHOP.
- General consistency of treatment effect was observed across exploratory subgroups, but cautious interpretation is advised.
- Five-year data confirm Pola-R-CHP as a standard of care for patients with previously untreated intermediate- or high-risk DLBCL; prolonged follow-up of POLARIX is planned.

Presented at the 13th Annual Meeting of the Society of Hematologic Oncology (SOHO 2025) | September 3–6, 2025

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2. Song Y, *et al. Blood* 2023;141:1971–81.

Acknowledgments

The POLARIX (NCT03274492) study team would like to thank all participating patients and their families, research staff, and the investigators.

Third-party medical writing assistance, under the direction of the authors, was provided by Anna Nagy, BSc of Ashfield MedComms, an Inizio company, and was funded by F. Hoffmann-La Roche Ltd.

Disclosures

GS: stock/other ownership (Oxkiri), honoraria (Incyte, Genentech/Roche, Merck), consulting/advisory role (AbbVie, ATB therapeutics, Beigene, BMS, Debiopharm, Genentech/Roche, Gemmab, Innate Pharma, Incyte, Ipsen, Janssen, Kite/Gilead, Loxo/Lilly, Merck, Modex, Molecular Partners, Nordic Nanovector, Novartis, Nurix, Orna Therapeutics, Treeline), speakers bureau (Incyte, Genentech/Roche, Merck), research funding (AbbVie, Genentech, Gemmab, Janssen, Ipsen); **FM:** honoraria (AstraZeneca, Kite/Gilead, Takeda), consulting/advisory role (AbbVie, BMS, Janssen, Millenry, Modex Therapeutics, Roche), research funding (BMS, Kite/Gilead, Roche); **LHS:** honoraria (AbbVie, Amgen, AstraZeneca, Beigene, BMS, Kite/Gilead, Incyte, Janssen, Merck, Roche/Genentech, Seagen), consulting/advisory role (AbbVie, Amgen, AstraZeneca, Beigene, BMS, Kite/Gilead, Incyte, Janssen, Merck, Roche/Genentech, Seagen), research funding (Roche/Genentech, Treos); **AFH:** consulting/advisory role (AbbVie, ADC Therapeutics, Alogene Therapeutics, AstraZeneca, BMS, Genentech, Gemmab, Merck, Pfizer, Seagen, Takeda), research funding (BMS, Genentech, Merck, Seagen); 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